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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/813,965

03/31/2004

Robert Falotico

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7706

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EXAMINER

KIM, JENNIFER M

ART UNIT

PAPER NUMBER

1617

MAIL DATE

DELIVERY MODE

09/16/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/813,965	Applicant(s) FALOTICO ET AL.	
	Examiner JENNIFER M. KIM	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on August 13, 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,5,9 and 10 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4 and 5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed March 16, 2009 have been received and entered into the application.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 13, 2009 has been entered.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sehgal (EP 0041795 A2) of record in view of Rubino et al. (US2004/0167152 A1) of record.

Sehgal teaches an injectable composition of rapamycin, suitable for intravenous administration comprising about 1 to 20mg/ml of rapamycin composition and nonionic

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surfactants. (page 19, claim 1). This concentration range encompasses Applicants' range set forth in claims 1 and 3. Sehgal teaches that the rapamycin composition is prepared by dissolving rapamycin in an organic solvent which is capable of dissolving rapamycin and is miscible with the nonionic surfactant such as ethanol, and adding the nonionic surfactant, if required, removing some or all of the organic solvent, and **adding water**. (page 6, line 4- page 7, line 5). Sehgal illustrates the preparation of an injectable rapamycin composition by removing ethanol by evaporation. (page 8, example 1, claim 7). Sehgal teaches that various surfactant can be employed in the composition. (page 3, claim 9).

Sehgal do not teach the amount of ethanol and vitamin E TPGS set forth in claim 1.

Rubino et al. teaches that the precipitation of rapamycin, particularly 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methyl-propionic acid (CCI-779) CCI-779 in a parenteral formulation can be prevented by use of the surfactant including vitamin E tocopherol propylene glycol succinate (Vitamin E TGPS). ([0021], abstract). Rubino et al. also teach that parenteral CCI-779 formulations can be formulated with the various concentrations of 0.05mg/ml, from 2.5mg/ml, from 5mg/ml, from 10mg/ml or from 25mg/ml up to approximately 50mg/ml.

It would have been obvious to one of ordinary skill in the art to incorporate vitamin E TPGS in Sehgal's parenteral rapamycin formulation because Sehgal teaches that various surfactants can be added in the formulation and because Rubino et al. teach that TPGS can prevent the precipitation of CCI-779 in a parenteral CCI-779

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formulation. One would have been motivated to make such modification in order to avoid the precipitation of parenteral rapamycin formulation taught by Sehgal et al. by adding surfactant such as TPGS taught by Rubino et al. There is a reasonable expectation of successfully formulating rapamycin together with TPGS because Sehgal teaches that various surfactants can be employed in rapamycin formulation and vitamin E-TPGS prevents precipitation of parenteral rapamycin formulation. With regard to the claimed residual content of residual ethanol content of 0.5% to less than 2%, such is obvious because Sehgal illustrates removing ethanol by evaporation upon the dissolution of rapamycin in the process of preparing the injectable formulation of rapamycin. Sehgal teaches that some or all of the ethanol content can be removed once the dissolution of rapamycin takes place. Therefore, the residual ethanol content of less than 2% is encompassed and obvious over the evaporation step involving removal of **some** of ethanol taught by Sehgal et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Response to Arguments

Applicants' arguments filed August 13, 2009 have been fully considered but they are not persuasive. Applicants argue that Sehgal discloses an injectable composition of rapamycin that comprises no vitamin E in the final product. This is not found to be

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persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Sehgal's injectable composition rapamycin with no vitamin E is cured by Rubino et al., who teach that addition of Vitamin E TGPS in the rapamycin formulation prevents the precipitation of rapamycin. Therefore, one would have been motivated to add the vitamin E TGPS in Sehgal's rapamycin injectable formulation in order to avoid the precipitation of rapamycin in the injectable formulation of Sehgal et al.

Applicants argue that Sehgal's injectable formulation is not a stable solution because the formulation has to be diluted shortly before administration. This is not found to be persuasive because one would readily recognize that upon addition of water to Segal's injectable formulation as modified by Rubin, the stability of the formulation would be increased due to addition of the advantageous surfactant such as Vitamin E TGPS which prevents the precipitation. One would have been motivated to combine these references and make such modification because they are drawn to same technical fields (constituted with same active ingredient and well known surfactant (e.g. vitamin E TGPS)), and pertinent to the problem which applicant concerns about (precipitation of rapamycin). MPEP 2141.01(a). Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/
Primary Examiner, Art Unit 1617

Jmk
September 4, 2009